

UNCINARIASIS IN PANAMA.

By G. H. WHIPPLE, M.D.,

ASSOCIATE IN PATHOLOGY IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE.

It is not the object of this paper to discuss the general pathological anatomy of fatal cases of uncinariasis, but rather to note the presence of hook-worms in the routine autopsy cases, and the fact that the old world hook-worm (*Ankylostomum duodenale*) and the new world hook-worm (*Necator americanus* or *Uncinaria americana*) are often present in the same case. A few points relating to the pathology of the jejunum will be discussed—especially hemorrhage and inflammation in the submucosa. No attempt will be made to review the literature which has been very carefully compiled by A. Looss.¹

During the year from September, 1907, to September, 1908, 420 autopsies were performed at the pathological laboratory of the Ancon Hospital, C. Z., Panama, and in the last 232 cases the intestinal parasites were studied with some care. In this series of 232 consecutive cases the presence of hook-worms was recorded in 72 cases (31 per cent.). In 39 cases no mention of intestinal parasites was made, but we feel sure that in these cases the hook-worm was absent. If, however, this number is deducted from 232, the percentage of cases infected with hook-worms rises to 37 per cent. The whites in this series numbered 37, with but 2 cases of uncinariasis, a frequency of only 6 per cent. Both cases were in Spaniards. The whites included Americans, Spaniards, Greeks, Italians, etc. The blacks came principally from the Southern West Indies and Central America. If we deduct the white cases, we find the frequency of hook-worm infection to be 36 per cent. Heavy infections with hook-worms were not common, and cases showing 100 or more worms occurred only five times in the 232 cases. Both old and new world varieties were present in every one of the severe infections, *Necator americanus* predominating. Of the entire 420 cases, only 9 showed a heavy infection—that is, over 100 worms. These cases came from Jamaica (3), Martinique (2), Costa Rica (1), Colombia (1), Antigua (1), and Guadeloupe (1). As the sanitary conditions on the canal zone are excellent and most of the laborers wear shoes, we may say that the great majority of these cases were infected in their native lands. The length of their stay on the Isthmus varies from one month to two years. Cases among native Panama negroes show light infections, but both types of the hook-worm are present.

The old world hook-worm (*Ankylostomum duodenale* or *Uncinaria duodenalis*) was present in 39 cases (17 per cent.), and in 25 cases was found associated with the new world variety (*Necator ameri-*

¹ Handbuch der Tropenkrankheiten, 1905, i, 116; Centralbl. f. Bact., 1907, xxxv, 752.

canus). The new world hook-worm was present in 49 cases (21 per cent.), and predominated in all heavy infections.

It is not a difficult matter to separate the two types of hook-worm. The parasites were washed in running water until clean, then placed in Petri dishes on a glass plate painted black. After some practice, one can separate the two types by using the lens of a dissecting microscope. The old world worm is thicker, and has a milky look. It is more active, and has a blunt head end. The mouth and œsophagus are over twice the size of those of the new world variety. The new world worm has a more delicate body, with a smaller head end and œsophagus. It has a more translucent appearance, except when containing blood. The two types of worms separated with the aid of a low-power lens are placed in saline solution in rows on slides and examined under a No. 3 objective (Leitz). The four prominent hooks found in the mouth of the old world worm are easily seen, and establish the diagnosis. In many cases the dorsal rays of the caudal bursa in the males were studied, as well as the location of the vagina in the females. *Ankylostomum duodenale* in appearance corresponds very closely with *Ankylostomum caninum*, which is present in great numbers in all the native dogs.

232 CASES: 37 WHITES; 195 BLACKS.

	White.	Black.	All Cases.
Hook-worms present	2 cases (6%)	70 cases (36%)	72 cases (31%)
Old world hook-worm, <i>Ankylostomum duodenale</i> . .	2 cases (6%)	37 cases (19%)	39 cases (17%)
New world hook-worm, <i>Necator americanus</i> . . .	2 cases (6%)	47 cases (24%)	49 cases (21%)
New and old world hook-worm together in same case .	2 cases (6%)	23 cases (12%)	25 cases (11%)
Whip-worm (<i>Trichuris trichiura</i>)	3 cases (8%)	37 cases (19%)	40 cases (17%)
<i>Ascaris lumbricoides</i>	(0%)	19 cases (10%)	19 cases (8%)

The following table comprises 62 cases, in which the worms were studied and classified. In some cases the males and females were not separated and numbered, but this was carefully done in the majority of cases. The intestinal tract opened, but not washed, was looked over by a laboratory assistant, who picked out most of the worms; then the person performing the autopsy examined it carefully and collected any remaining parasites. We feel sure that very few worms escaped this routine examination. Whip-worms and round-worms were recorded in the 232 cases. Whip-worms were present in 40 cases (17 per cent.)—three of the cases were in white patients. *Ascaris* infection was found in but 19 cases (8 per cent.), all in black patients; 134 cases were free from intestinal parasites (58 per cent.).

Home.	Uncinaria.				Whip-worm.	Ascaris.	Remarks.
	Americana.		Duodenalis.				
	F.	M.	F.	M.			
Jamaica	91	43	17	4			Worms contain fresh blood.
Jamaica	60	26	3	1			Worms contain fresh blood; many submucous ecchymoses.
Jamaica	2	2	16	22			Worms contain fresh blood.
Jamaica	(20)						
Jamaica	2	1			1		
Jamaica	2	4					
Jamaica	4	2					
Jamaica	1				2	1	
Jamaica			(3)				
Jamaica	(8)						
Jamaica		1				1	
Jamaica	+		+		+		
Barbadoes	14	5	3	2	3		Many submucous hematomas.
Barbadoes	8	2	1		1		
Barbadoes	2	2	6				
Barbadoes	2	1			1		
Barbadoes	(5)						
Barbadoes			2	4	1		
Barbadoes			2	2			
Barbadoes	3						
Barbadoes			1				Many submucous hematomas.
Barbadoes			1			2	
Barbadoes	(1)						
Barbadoes			1				
Barbadoes	Few hook-worms.						Many submucous hematomas; blood cyst contains hook-worm.
Barbadoes			+				Worms contain fresh blood.
Martinique	(200)		3	4			Many submucous ecchymoses, worms contain fresh blood; small blood clots adherent to mucosa.
Martinique	82	77	9	8	1		Worms contain fresh blood.
Martinique	9	6	4		1		
Martinique	10	4			6		
Martinique	3		15	4	1		
Martinique	3	1			9		
Martinique			2				
Martinique	(1)		(1)				
Martinique	+		+				Many submucous hematomas; blood cyst contains hook-worm.
Antigua	(100)		(60)				
Antigua	2		(30)				
Antigua			1	1			
Grenada	(38)		(1)				
Grenada	(35)		(2)				
Grenada			1				
Gaudeloupe	(11)		1	1	2		
Gaudeloupe	(6)				1		Many submucous hematomas; blood cyst contains hook-worm.
Trinidad	19	9	25	30			Many submucous ecchymoses;
St. Vincent	6	5			1	2	many submucous hematomas;
St. Lucia	(1)				1		small blood clots adherent to mucosa.
	6	3					Many submucous hematomas;
Spain	(20)		(3)				blood cyst contains hook-worm.
Spain	2	2	3		3		
Cuba	2						
Panama	(75)						
Panama	(10)		(2)		12	1	
Panama	11	3	1	1	1		Worms contain fresh blood.
Panama	8	2				12	
Panama			2	1	4		
Panama				1			
Colombia	23	19			3		
Colombia	8	7	1				
Colombia			(2)			3	
Colombia	1						
Costa Rica	1		1				Worms contain fresh blood; many submucous hematomas.
Costa Rica	(100)		(10)		3		Many submucous ecchymoses; worms contain fresh blood.

A glance at the table under "Remarks" will show that our findings do not correspond with those of Ashford and King,² in Porto Rico, concerning intestinal ecchymoses and the presence of blood in the digestive tract of the hook-worms. They state that ecchymoses are very rare, only a few being found in a single case in their series, and that the worms very rarely contain blood.

Ecchymoses in the mucosa or submucosa were a common finding in the jejunum infected with hook-worms, both at the point of attachment of the worm's head and in other places where presumably the worm had been feeding. When the area of hemorrhage exceeded 3 to 4 mm. in diameter, it was referred to as a "submucous hematoma." A note of "ecchymoses" or "submucous hematomas" was made in 18 cases, and in several cases they were very numerous (No. 1441), giving a speckled appearance to the mucosa.

The blood cysts described by Bilharz and Grassi were not infrequent, and were often found with an included hook-worm—7 cases (Figs. 1 and 2). Such cysts measured from 5 to 10 mm. in diameter; more rarely the worm was completely buried in the submucosa with very little extravasation of blood (Fig. 2). Sections show great numbers of large intestinal bacilli associated with the worms buried in the submucosa, and these bacteria cause an extensive inflammation of the adjacent mucosa and submucosa which are infiltrated with large numbers of polymorphonuclear leukocytes and eosinophiles.

This series of cases shows that the worms often contain fresh blood, both the new and old world forms, more frequently the latter. A note that "many worms contain fresh blood" was made in 16 cases, and it was unusual not to find a few worms containing blood in an infected case when the autopsy was performed within two or three hours after death. It was noted that in cases of advanced anemia the worms rarely contained blood, while in cases showing no anemia the worms very often contained fresh blood and ecchymoses were more evident. This may explain the findings of Ashford and King, who maintain that the hook-worms very rarely contain blood. These writers examined fatal cases of uncinariasis which showed extreme anemia. When worms which were full of bright blood were removed from the intestinal mucosa and placed in water or 0.8 per cent. saline solution, they soon discharged the blood. Under the microscope one could watch the red blood cells and blood-stained fluid being poured out from the mouth and anus. This explains the fact that worms found in the feces or at an autopsy performed several hours after death may contain very little or no fresh blood.

Looss and others insist that the worms live on the intestinal epithelium, and cannot digest the blood. It seems rather hasty to

² Jour. Amer. Med. Assoc., 1907, xlix, 471; Boston Med. and Surg. Jour., 1907, clvi, 415; Report of the Commission for the Study and Treatment of Anemia in Porto Rico.

decide that a worm can digest epithelial cells from the human host, yet cannot digest red blood cells.



FIG. 1.—Blood cyst below the mucosa of the jejunum, with cross-section (a) of included hook-worm.



FIG. 2.—Hook-worm in the submucosa, with very little extravasation of blood; cross-section of the body of a female worm.

The following fact proves that the hook-worm can live and thrive for a considerable length of time in blood. Hook-worms removed from the "blood cysts" in the intestinal mucosa were invariably very active and vigorous and contained fresh blood. Sections through some of these "cysts" showed an invasion of the blood and adjacent submucosa by leukocytes and various wandering cells in considerable numbers. Such a reaction required from two to four days, during which time the worm lived in the blood and ingested more or less of it, as can be seen in sections which show the

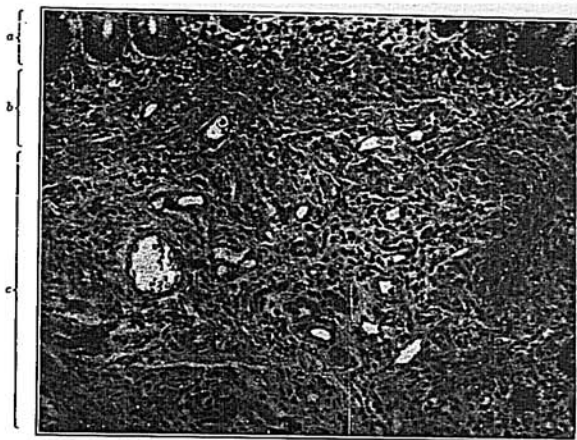


FIG. 3.—Jejunum in a fatal case of uncinariasis, showing extensive scarring and inflammation of the intestine. (a) Bases of crypts of Lieberkühn; many polymorphonuclear leukocytes in the interglandular tissue; (b) muscularis mucosae distorted and scarred, invaded by many wandering cells, many of them eosinophiles; (c) submucosa, which is much thickened and full of every type of cell—eosinophiles, polymorphonuclears, and "polyblasts." There is much scar tissue; new-formed bloodvessels are seen.

worm's intestine to contain red cells and granular detritus. It is admitted by all writers that blood is found in the worm's intestine, and it seems reasonable to conclude that the parasites live on both the blood and the epithelium, but we feel sure that the blood is the main factor when the worms are feeding on a fairly normal mucosa. In a heavily infected case, when the mucosa is very anemic, somewhat thickened, and infiltrated with leukocytes (Fig. 3), it is fair to suppose that the worms may live chiefly on the epithelium and mucus. Sections of worms show the intestinal canal containing red blood cells, coagulated albuminous detritus, and epithelial cells.

Many writers (Ashford, Baker,³ Yates⁴) believe that uncinaria produces some obscure hemolytic toxin analogous to that of *Bothriocephalus latus*, but this has never been demonstrated. Clinically, too, the blood pictures are very different (Boycott,⁵ Adami⁶), as the anemia of uncinariasis is distinctly of the secondary type. I hope to show in another article⁷ that the hook-worm of man does contain a hemolytic factor which is constant but very weak. It is present in all parts of the worm, probably in the intestinal canal—not in the cephalic glands alone.

That the hook-worm does not contain a powerful hemolysin is shown by a study of the "blood cysts" described above (Fig. 1). The worms often remain in these sumbucous blood clots for a few days at least, as shown by the number and type of wandering cells in the edge of the clot. The worms are not injured by their stay in the blood, yet there are well-preserved red blood cells in all parts of the "blood cysts." It seems that this is almost a perfect experiment performed by the hook-worm: the parasite is included in a small sac of the host's blood, and all conditions are as they should be to demonstrate the presence of a hemolytic agent—yet the blood cells are not dissolved in any great number. Here we have a small amount of blood isolated in the human tissues and containing an active hook-worm. In many cases there is less than 0.5 c.c. of blood in the cyst, and the parasite lives in this medium one, two, or three days, yet can cause no marked hemolysis. The parasite by its activity has deprived its host of a fraction of a cubic centimeter of blood, but cannot hemolyze this small amount during a considerable interval of time. Thus, the worm can cause the loss of more blood through damage to the mucosa than it can hemolyze under favorable conditions. It does not seem likely, therefore, that this same worm could secrete a hemolytic substance which, taken up by the human intestine, could act on the circulating blood, where surely conditions would be less favorable for hemolysis than in the "blood cysts." I believe that this observation alone is sufficient to exclude the presence of a powerful hemolysin in the hook-worm—a hemolysin which could be absorbed by the host and cause an advanced secondary anemia.

The cause of the anemia is not clear: various explanations have been advanced. Some writers disregard the blood abstracted by the worm, and the numerous "bites" which often bleed after the worm has changed its feeding ground (No. 1441). Loeb⁸ has demonstrated a substance, which definitely inhibits the blood coagulation, to be present in the cephalic glands of *Ankylostomum caninum*, and this may be a factor in promoting the oozing of blood from the

³ Brit. Med. Jour., 1903, i, 718.

⁴ Johns Hopkins Hosp. Bull., 1901, xii, 364.

⁵ Brit. Med. Jour., 1907, ii, 1318; Jour. Hyg., January, 1904, iv, No. 1.

⁶ Montreal Med. Jour., 1903, xxxii, 186.

⁷ Jour. Exp. Med., 1909, xi, No. 2.

⁸ Proc. Path. Soc., Philadelphia, June, 1904; Centralbl. f. Bact., 1906, xi, 740.

mucosa. It has been proved that this worm is a bloodsucker, and the daily abstraction of a small amount of blood cannot be disregarded. Many writers attribute the anemia to an obscure toxin produced by the cephalic glands of the worm and absorbed by the host. No proof of the existence of any such toxin has been furnished, and until this proof is forthcoming such an explanation is merely evading the question.

Others (Ferguson)⁹ have advanced the theory that the "bites," which are always greater in number than the parasites, cause little foci of infection in the mucosa, a chronic inflammation, and anemia. The anemia may be due to the poisonous products absorbed from these foci of inflammation in the intestine. This, I believe, is the most important factor in the production of the anemia, and explains the fact that some cases with relatively few uncinariae may show a profound or even fatal anemia. Case 1137 may be cited as an example of this: A male, Jamaican, negro, aged sixty years, shortly before his death, had 15 per cent. of hemoglobin. There was nothing unusual about the gross pathology of the viscera. The tissues were all very pale. The heart was greatly dilated, with watery, pale clots—hydremia. The lungs were pale and cushiony. The liver and kidneys showed a definite yellowish brown pigmentation and anemia. The bone marrow was very firm, pink, and cellular. The jejunum contained between 100 and 200 hook-worms, but the types were not identified. The mucosa was very pale and smooth. There were no notes concerning the presence of fresh blood in the worms, and no notes regarding ecchymoses. We cannot assume that the worms were discouraged by the anemia, abandoned the mucosa, and were carried out in the feces, for we find cases with even greater anemia and many hundreds of worm in the intestines. Microscopic sections of this jejunum are most interesting (Fig. 3). The mucosa shows rather short villi and crypts, with a little distortion of the architecture of the glands, due to an increase in connective tissue. The interglandular tissue in the villi and at the base of the gland tubules shows a marked infiltration with polymorphonuclear leukocytes and eosinophiles, which in some fields are more numerous than the mononuclears. The muscularis mucosæ is thickened, scarred, and infiltrated with wandering cells of all types. The submucosa is thickened and scarred. It is not sharply separated from the muscularis mucosæ, and many polymorphonuclear leukocytes and eosinophiles are present. Accumulations of large mononuclear wandering cells are found about the vessels in the submucosa. The outer muscle coats are normal. This is a very definite pathological change, a picture of diffuse inflammation, evidently of some duration, due to the hook-worm, as evidenced by the eosinophiles.

When one considers the amount of tissue which was involved in this

⁹ Brit. Med. Jour., 1907, II, 1320.

change—several feet of the jejunal mucosa—it is not difficult to account for an advanced anemia. Perhaps the same explanation may hold for the liver necroses which were present in this case, and similar to those described by Yates in a fatal case of infection with the new world hook-worm. Many of the liver lobules show a necrosis of the central half or third, where the liver cells are quite hyaline, and wandering cells are invading such areas. The other liver cells show some fatty infiltration, and a deposit of a finely granular, yellow pigment.

Reasoning from this series of cases, it seems probable that the anemia of uncinariasis is due to two factors at least: (1) Loss of blood through feeding of the worms and oozing from damaged areas where the worms have broken the mucosa; and (2) infection of the intestinal mucosa and submucosa, due to bites of the worms which give points of entrance for intestinal bacteria.

SUMMARY. 1. Hook-worms are found in the routine autopsy examinations in 31 per cent. of the cases.

2. The old world hook-worm (*Ankylostomum duodenale*) is present in 17 per cent. of the cases, together with *Necator americanus* in 11 per cent. of the cases.

3. The new world hook-worm (*Necator americanus*) is present in 21 per cent. of all the cases, and predominates in all heavy infections.

4. The whip-worm (*Trichuris trichiura*) is present in 17 per cent., and *Ascaris lumbricoides* in 8 per cent. of the cases.

5. Hook-worms removed from the intestinal mucosa a few hours after the death of a patient very often contain fresh blood.

6. Ecchymoses and small submucous hematomas are not rare findings in an infected jejunum.

7. Hook-worms ingest both blood and epithelial cells and presumably digest both.

8. The anemia is due not only to direct loss of blood through activity of the hook-worms, but to a diffuse inflammation of the mucosa and submucosa of the jejunum. This inflammation is caused by the bites of the parasites which damage the mucosa and give entrance to the intestinal bacteria.

9. The severity of the anemia depends upon the number of hook-worms, and upon the intensity and extent of this diffuse inflammation. This second factor may explain the cases of fatal anemia in which only relatively few hook-worms are present.

10. Study of the "blood cysts" containing hook-worms shows that the parasites can live in blood for days and cause no active hemolysis of this blood—strong evidence against the presence of a powerful hemolysin in the hook-worm.

In conclusion, it is a pleasure to express my sincere thanks to Colonel W. C. Gorgas and Dr. S. T. Darling, for permission to use the material at the Ancon Laboratory, and to Dr. A. H. Dodge, who assisted in much of the routine work.